International Preliminary Examination Authority
European Patent Office
Erhardtstraße 27
D-80298 München
GERMANY

18 January 2006

Dear Sirs

PCT Patent Application No PCT/GB2005/000751
PROTHERICS MOLECULAR DESIGN LIMITED
Our Ref: PROBV/P32598PC

This is in response to the written opinion of the ISA dated 26 October 2005.

Amendments

We enclose replacement pages 45-50 to replace these pages currently on file. We also enclose hand-amended copies of previous pages 45-50 to allow the amendments to be more clearly identified.

Previous Claim 31 has been deleted, and the subsequent claims have been renumbered accordingly.

Claim 44 (previously Claim 45) has been amended to specify that the medicament is for combating toxicity caused by the antifolate compound of Formula I. This has basis throughout the application as filed, for example in Claim 1 as filed, page 16 last paragraph, and on page 23 lines 29-30.

Thus, these amendment do not add new matter.

Clarity

3. We do not agree with the examiner that Claim 1 lacks clarity. All of the steps required to carry out the method of Claim 1 are perfectly clear. The examiner appears to require that a mechanism of action "wherein the carboxypeptidase G activity is effective to combat toxicity caused by said antifolate compound" is included in Claim 1. We are not aware of any requirement under the PCT to support this position by the examiner. Similarly, we do not agree that it is necessary to amend Claim 36

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(previously Claim 37) to specify a mechanism of action. Certainly, such amendments would not be required in the majority of territories in the national and regional phases.

4. We have deleted Claim 31.

5. We have amended Claim 44 (previously Claim 45) to clarify that the medicament is for combating toxicity caused by the antifolate compound of Formula I.

6. We wish to point out that Claims 31-44 are all second medical use claims. Non-assessment of industrial applicability is normally limited to methods of treatment.

Any amendment is not to be construed as abandonment of subject matter.

Should the examiner be inclined to issue an IPER that is not completely favourable, we request, in order of preference, a further written opinion, or a telephone interview, first.

Yours faithfully

JSM

John S Miles PhD hs
For and on behalf of Eric Potter Clarkson LLP

Enc: Replacement pages 45 to 50 (retyped)
Replacement pages 45 to 50 (hand-amended)